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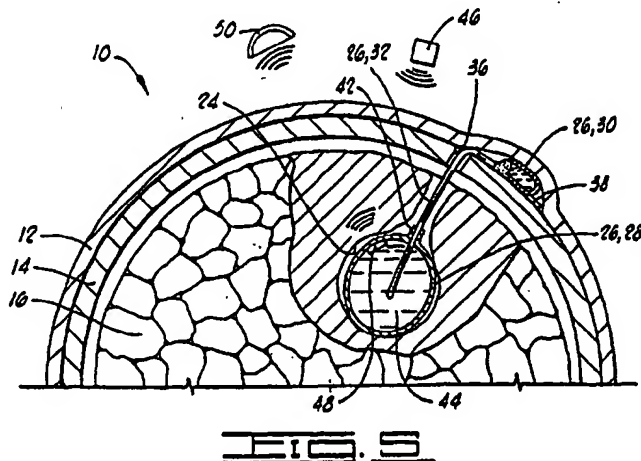
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under INID code 62.

### (54) Tumour treatment apparatus

(57) A chemotherapy apparatus (10) for treatment  
of tissue surrounding a cavity (24) left by a surgical exci-  
sion, comprises:

a distensible inner reservoir (28A) and outer reser-  
voir (28B), the outer reservoir comprising a porous  
wall and the inner reservoir comprising a non-  
porous wall, the inner and outer reservoirs

arranged so that a space is defined between them;  
a first catheter (32) connected to the space  
between the inner and outer reservoirs for delivery  
of a chemotherapy fluid into the space; and  
a second catheter (72) connected to the inner res-  
ervoir for delivery of a second fluid into the inner  
reservoir.



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## Description

[0001] The present invention relates to apparatus for the treatment of tumours in a living body, and more particularly, but not by way of limitation, to apparatus for treatment of brain tumours in a human.

[0002] Conventional techniques of post-operative treatment of residual tumour following only gross removal of tumour include sequential, but not simultaneous administration of radiation, chemotherapy, and/or heat. Simultaneous administration of these modalities to the residual tumour is advantageous but impossible utilizing currently available techniques.

[0003] Further, no currently available intraoperative therapeutic procedure utilizes the cavity formerly occupied by the bulk of the tumour for placement of an inflatable device for subsequent tumour therapy, whether combined (radiation and/or chemotherapy and/or hyperthermia together) or single modality (one of the above alone), or whether simultaneous or sequential in application.

[0004] The current practice of brachytherapy (implantation of radioactive sources in the tumour and surrounding tissue) requires simultaneous placement of numerous separate catheters. Placement of catheters for afterloading must currently incorporate pre-operative placement of a stereotactic frame for localization, a procedure which is expensive, cumbersome, and time-consuming. In frame placement, a large heavy frame is attached to the skull of the awake patient utilizing transdermal metal screws and local anaesthetic, often not a smooth or desirable procedure. Once the frame is placed, a CT scan and extensive calculations are required before the patient is transported to the operating room, with the frame on his or her head, for the actual catheter placements. This second transport is cumbersome.

[0005] Once in the operating room, numerous separate holes (usually up to 24) are manually drilled in the patient's scalp and skull. Then existing catheters are placed to the appropriate depth and sewn in place. These catheters are subsequently afterloaded with solid isotopic pellets for a prescribed time. The pellets are removed and, if hyperthermia is desired, separate metal antennae are loaded into the existing catheters for subsequent heating and thermometry. Although reasonably proximal in time, these sequential loadings reduce the efficacy of combined treatment, which should be simultaneous for highest tumour kill. During treatment, the catheters are externally exposed with attendant risk of infection.

[0006] Following delivery of the prescribed radiation and heat, the catheters are removed. Any subsequent treatment, as for example following tumour recurrence, would require repeating the entire sequence described above.

[0007] US-A-4816016 discloses an implantable apparatus for treatment of tissue surrounding a cavity left by

surgical removal of a tumour from a living patient, comprising an inflatable balloon adapted to be placed in said cavity, and a catheter means for conducting treatment fluid to said inflated balloon.

[0008] WO 90/04365 and WO 91/05528 disclose an implantable for treatment of tissue surrounding a cavity left by surgical removal of a tumour from a living patient, comprising an inflatable balloon adapted to be placed in said cavity, a catheter means for conducting treatment fluid to said inflatable balloon, and heating means operatively associated with said balloon for heating said treatment fluid while said treatment fluid is in said balloon.

[0009] Starting from the disclosure of these two documents, the present invention said heating means comprises a chemotherapy apparatus for treatment of tissue surrounding a cavity left by a surgical excision, comprising:

a distensible inner reservoir and outer reservoir, the outer reservoir comprising a porous wall and the inner reservoir comprising a non-porous wall, the inner and outer reservoirs arranged so that a space is defined between them;

a first catheter connected to the space between the inner and outer reservoirs for delivery of a chemotherapy fluid into the space; and

a second catheter connected to the inner reservoir for delivery of a second fluid into the inner reservoir.

[0010] The apparatus of the present invention is non-invasive and does not require the use of wires extending out through an aperture in the patient's body.

[0011] The apparatus of the present invention thus provides the possibility of simultaneous heat therapy and therapy by treatment flow.

[0012] The treatment flow can be radioactive treatment fluid or a chemotherapy fluid, or in one embodiment a double-wall balloon is provided so that both a radioactive treatment fluid and a chemotherapy fluid can be simultaneously applied.

[0013] Monitoring means may be provided for monitoring the temperature of the treatment fluid in the balloon.

[0014] The invention provides a significant advantage in that it provides a means for simultaneous administration of radiation therapy and/or chemotherapy and/or heat therapy.

[0015] Another advantage is that a treatment device is intraoperatively placed in the cavity formerly occupied by the bulk of the tumour thus providing a means for subsequent treatment of residual tumour without further surgical incisions.

[0016] Another advantage is that the distensible balloon takes advantage of the inherent natural compliance of a fluid to conform to the outline of the cavity to be treated, thus allowing close approximation of the treatment device to the treated residual tumour.

[0017] The present invention also takes advantage of

the greater variety of desirable physical or superior cost properties inherent in readily available liquid isotopes. These liquid isotopes are cheaper and possess higher specific activities (millicuries per gram) when compared to their conventional, solid counterparts. This is a highly desirable characteristic which allows a higher concentration of radioactivity to be administered, thus resulting in higher tumour cell kill.

[0018] Another advantage of the present invention is that it allows homogeneous mixing of disparate treatment agents for the uniform administration of hyperthermia and brachytherapy simultaneously to a human tumour surrounding a post-operative cavity.

[0019] Numerous other objects, features and advantages of the present invention will be readily apparent to those skilled in the art upon a reading of the following disclosure when taken in conjunction with the accompanying drawings.

Figs 1-4 comprise a sequential series of schematic elevation sectioned drawings through the coronal portion of the head of a human being. In Fig. 1 the scalp has been laid back and one or more burr holes are placed in the skull allowing creation of a circular bone flap which when temporarily removed allows gross resection of the tumour. In Fig. 2 the major portion of a brain tumour has been operatively removed. In Fig. 3 intra-operative placement of the implantable apparatus of the present invention has been accomplished and the incision has been closed. In Fig. 4 a hypodermic needle is used to transdermally place a treatment fluid in the apparatus to inflate the distensible catheter in place within the cavity formed by removal of the tumour.

Fig. 5 is an enlarged view similar to Fig. 4 illustrating further details of the apparatus including means for heating and means for monitoring the temperature of the fluid in the balloon.

Fig. 6 is a view similar to Fig. 5 illustrating alternative means for heating.

Fig. 7 is a view similar to Fig. 5 illustrating an alternative embodiment of the invention having a double-wall balloon to allow chemotherapy treatments.

Fig. 8 is a view similar to Fig. 5 of another alternative embodiment which is not completely implantable, and which has the catheter extending through a bolt means placed in the skull.

Fig. 9 is a view similar to Fig. 5 of another alternative embodiment having a treatment fluid receptacle countersunk within the skull so as to avoid deformation of the overlying scalp. The implantable receptacle includes a metallic ring which is visible to X-rays.

Fig. 10 schematically illustrates the placement of a metallic wire grid over the patient's scalp, with the metallic ring of the device of Fig. 9 being shown in dashed lines as it would be seen in a subsequent en face X-ray of the patient's scalp for purposes of

locating the receptacle.

[0020] In Fig 1 the coronal portion of the head of a human patient is shown and generally designated by the numeral 10. The patient's scalp 12 overlies the skull 14 within which is seen the brain 16. A tumour 18 is schematically illustrated within the brain tissue 16. The scalp 12 has been laid back as indicated at 20 and one or more burr holes have been cut to allow creation of a bone flap (not shown) which is removed to form an access opening 22 in the skull thus providing operative access to the brain 16 and the tumour 18.

[0021] In Fig. 2, the bulk of the tumour 18 has been operatively removed thus leaving a cavity 24 within the remaining brain tissue 16 which will include some residual tumour immediately surrounding the cavity 24.

[0022] In Fig. 3, the implantable treatment apparatus 26 has been intra-operatively implanted prior to closure of the surgical incisions. The apparatus 26, as better seen in Fig. 5, includes an inflatable balloon 28 constructed for placement in the cavity 24, a subcutaneously implantable treatment fluid receptacle means 30, and a catheter means 32 connected between the receptacle means 30 and the balloon 28 for carrying treatment fluid from the receptacle means 30 to the inflatable balloon 28.

[0023] The assembly of the implantable apparatus 26 is generally as follows starting with the subcutaneous receptacle 30 and moving distally. The various connections discussed in the following description are not shown in detail in the figures, but comprise conventional widely acceptable neurosurgical techniques and will be well understood by those skilled in the art. An outlet connector extends outwardly from the subcutaneous receptacle 30 and engages an end of the siliconized plastic surgical tubing comprising the catheter 32 in a manner like that shown in Fig 7 of U.S. Patent No. 4,681,560 to Schulte et al. The end of the outlet connector from the subcutaneous receptacle 30 includes a flange portion which sealingly engages a suture sleeve to form a seal preventing medication from exiting the assembly other than through the connector leading to the catheter 32.

[0024] In order for the catheter 32 to make the right-angle turn downward through burr hole 36 as illustrated in Fig. 5, a plastic right-angle device (not shown) which causes the catheter tube 32 to be conformed to a right angle can be placed around the tube at the time of installation at the proper linear dimension along the tube. Thus, depending upon the necessary distance between the subcutaneous receptacle 30 and the burr hole 36, the right-angle device may be located closer to or further from the subcutaneous receptacle 30. These assembly techniques just described confer considerable flexibility in the placement and installation of the various components of the treatment device 26.

[0025] In Fig. 3, the apparatus 26 has been implanted with the balloon 28 located within cavity 24 but still in its

uninflated state. The access opening 22 has been closed by replacement of the previously removed bone flap. The catheter means 32 is placed through a burr hole 36 which may have been formed when the bone flap was formed, or which may be specially formed in any desired location. The subcutaneous receptacle 30 has been placed on top of the skull 14 and the scalp 12 has been sutured back in place thereover. The receptacle 30 may include a suture tab such as 38 (see Fig. 5) allowing it to be sutured in place to the surrounding galea which is a tough overlying tissue which lies over the skull 14.

[0026] In Fig. 4 a hypodermic needle 40 is illustrated as transdermally injecting a treatment fluid into the subcutaneous implanted receptacle 30. The injection receptacle 30 includes a rigid base and an overlying self-sealing dome which encloses and defines an injection chamber. The self-sealing dome is constructed of a silicone elastomer material, such materials providing an acceptable level of tissue reaction when subcutaneously implanted, which can be pierced by a 25 gauge or smaller needle without affecting ability of the dome to reseal after the needle is withdrawn. The fluid from needle 40 flows through the catheter 32 to inflate the balloon 28 so that it substantially fills the cavity 24 thus placing the treatment fluid in close proximity to the remaining tumour in the brain tissue 16 surrounding the cavity 24. The walls of balloon 28 can generally be described as being in direct apposition with the remaining residual tumour tissue surrounding cavity 24. As further described below, various treatment modalities may be applied either individually or simultaneously.

#### The Embodiment of Fig. 5

[0027] Fig. 5 illustrates the apparatus 26 in a view similar to that of Fig. 4 but enlarged and showing further detail.

[0028] The subcutaneously implanted receptacle means 30 is constructed in a manner so that it can be easily and safely injected with the treatment fluid, and it is constructed of a material which will readily reseal upon withdrawal of the hypodermic needle. It may for example be constructed similarly to the subcutaneously implantable infusion reservoir shown and described in Schulte et al., U.S. Patents Nos. 4, 816, 016 and 4,681,560. It may also be an Onmaya CSF Reservoir such as is available from American Heyer-Schulte. The design of the subcutaneously implantable reservoir 30 should be small enough to minimize the volume or radioactive treatment fluid 44 in the subcutaneous area, but should be large enough to allow easy localization by palpation to facilitate loading with the hypodermic syringe 40. The subcutaneous receptacle 30 should be malleable and flexible to allow external palpation, but should be rigid enough that external compression cannot drive fluid from its interior into the catheter 32 and balloon 28. If compression should occur, the resilience

of subcutaneous receptacle 30 should provide for re-expansion, thus reaccumulating any fluid driven distally as noted above.

[0029] The catheter means 32 is constructed of conventional flexible plastic catheter materials.

[0030] The inflatable balloon 28, which may also be referred to as a distensible reservoir 28 or distensible catheter 28, is preferably constructed of flexible siliconized plastic and is attached to the catheter means 32 location 42 by a flanged plastic connector and multiple interrupted surgical ties.

[0031] Although the term "balloon" is used to describe the distensible reservoir 28, it will be appreciated that the material from which the balloon wall is constructed need not be an elastic material. It is only required that the reservoir 28 be capable of somewhat collapsing in size so that it can be easily placed in cavity 24 as shown in Fig. 3 and that it then subsequently fill with fluid so as to substantially fill the cavity 24. The fluid inside balloon 28 is not necessarily pressurized, although it may be. The collapse of the balloon 28 following treatment will allow easy removal of the catheter 32 and balloon 28 through an exiting burr hole 36 without first removing the entire bone flap should removal of the device be required for any reason.

[0032] In one preferred embodiment the treatment fluid 44 is a radioactive treatment fluid. The radioactive treatment fluid can be injected into the balloon 28 and left there for a prescribed period of time. Then it may be removed by reinserting hypodermic needle 40 into receptacle 30 and pulling a vacuum with the plunger of hypodermic needle 40 to cause the treatment fluid to flow back out of balloon 28 through catheter 32 into receptacle 30 and into the cylinder of hypodermic needle 40, so as to end the radiation treatment. Preferred radioactive isotopes for use in this procedure include 90-Yttrium, 198-Gold, 32-Phosphorous, 125-Iodine and 131-Iodine. The use of isotopes in liquid form allows considerable flexibility in administered dose rate in rad/hour and range (in millimetres) of the radioactive particles used in irradiating the residual tumour. Also with this apparatus a much more homogeneous dosage of radiation is applied to the surrounding tissue 16 than with the typical prior art devices described.

[0033] It is noted that since the apparatus of 26 can be loaded with radioactive solution after the completion of surgery there is much less danger of radiation exposure to operating room personnel than with the prior art techniques described above.

[0034] Of course for treatment with radioactive fluid 44, the balloon 24 would be made of non-porous material. For other treatment modalities, namely chemotherapy, a balloon 28 constructed of porous material may be utilized in a manner similar to that described below with regard to the porous outer wall 28A of Fig. 7, in order to allow the chemotherapy fluids to seep through the balloon 28 into actual contact with the surrounding brain tissue. When a porous balloon wall 28 is used for chem-

otherapy, so that there is no need to ever withdraw the treatment fluid from the balloon 28, the treatment device 26 may further include a check valve (not shown) disposed in catheter 32 similar to valve 82 of Fig.7 so that fluid can flow to balloon 28 but not back therefrom.

[0035] It is noted that the inflatable balloon 28 is preferably constructed so that it has an inflated volume as seen in Fig. 5 which is no greater than, and preferably slightly less than, the volume of the cavity 24 thus providing a means for avoiding any compression or distortion of the normal brain tissue 16 surrounding the cavity 24. It will be appreciated, of course, that distortion of the normal brain tissue can cause undesired complications.

[0036] Fig.5 also illustrates a first form of heating means 46 operatively associated with the balloon means for 28 for non-invasive heating of the treatment fluid 44 while the treatment fluid 44 is in the balloon 28. The heating means 46 illustrated in Fig.5 may either be an external ultrasonic transmission means 46 or an external radio frequency electromagnetic energy transmission means 46.

[0037] If the heating means 46 is an external ultrasonic transmission means, it focuses ultrasonic energy on the treatment fluid 44 in balloon 28. In the case of using ultrasonic energy to heat the balloon contents, the skull bone tissue 14 will not be replaced over the burr hole 22 thus providing a path for unimpeded transmission of the ultrasonic sound energy through the burr hole 22.

[0038] If the heating means 46 is an external radio frequency electromagnetic energy transmission means, the treatment fluid 44 will contain an iron oxide suspension in addition to the radioactive isotope in solution. This iron oxide suspension will be heated by the radio frequency electromagnetic energy.

[0039] A monitoring means 48 is provided for monitoring a temperature of the treatment fluid 44 within the balloon means 28. In a preferred embodiment, the monitoring means 48 is a crystal oscillator 48 implanted within the balloon means 28. The oscillator 48 may also be mounted on the outside of catheter 32 within the balloon 28. The crystal oscillator 48 has a frequency of oscillation which varies proportionately to its temperature. The frequency of oscillation of the crystal oscillator means 48 can be determined non-invasively by an external antenna 40 which may be considered to be a part of the monitoring means. The crystal oscillator 48 is available under the trade name CorTemp from Human Technologies Inc of St. Petersburg, Florida, such as described in "NASA Tech Briefs", June 1990, at page 106.

[0040] The system shown in Fig.5 when using a non-porous balloon 28, provides a means for simultaneous application of both radioactive therapy and heat therapy to the remaining brain tissue 16 surrounding the cavity 24.

[0041] In its broadest aspects, the surgical procedure utilizing the apparatus of Fig.5 can be described as

including steps of surgically removing at least a portion of the tumour 18 thereby creating the cavity 24 in the remaining brain tissue 16. Subsequently the treatment device 26,28 is placed in the cavity 24 and the remaining tissue 16 including residual tumour surrounding the cavity 24 is treated by means of the treatment device 25,28. The treatment device 28 preferably is an inflatable balloon 28. The inflatable balloon is inflated with a treatment fluid 44 so that the inflatable device 28 occupies the cavity 24 thereby placing the treatment fluid 44 in close proximity to the remaining tissue 16 surrounding the cavity 24. By use of the subcutaneously implanted receptacle 30 and transdermal injections of treatment fluid as indicated in Fig.4, the procedure can be performed non-invasively without making further surgical incisions on the patient. Although the apparatus and process of the present invention have been disclosed in the context of treatment of brain tumours, it will be appreciated that they can be used in connection with other types of tumours wherein treatment can be accomplished by placing the treatment device in a cavity left by removal of the tumour.

[0042] The entire apparatus 26 can be left in place permanently allowing subsequent further treatment as desired.

#### The Embodiment of Fig.6

[0043] Fig.6 illustrates an alternative embodiment providing a different means for heating the treatment fluid 44 within the balloon 28.

[0044] The system shown in Fig.6 utilizes an external microwave transmitter 52, and a subcutaneously implantable microwave receiver means 54. The microwave transmitter 52 preferably operate in the 200 MHz to 400 MHz range, and more preferably operates at about 300 MHz. The microwave receiver means 54 includes a metallic element 56 which actually receives the microwave energy and heats up. The microwave transmitter 52 may also be replaced by an ultrasound transmitter focussed on receiver means 54. Insulation 58 both overlies and underlies the metallic element 56 to prevent heating of the scalp 12 and underlying skull tissue 14. Suture tabs 60 may be used to attach the microwave receiver apparatus 54 to the skull 14.

[0045] A conductor means 62 extends from the metallic element 56 into the interior of the balloon 28 for conducting heat from the metallic element 56 into the treatment fluid 44 in the balloon 28. The conductor means 62 has external insulation 64 which covers a metallic conductor 66 a portion of which is uncovered inside of the balloon 28. Alternatively the conductor means 62 could be run through the hollow catheter 32.

[0046] The system of Fig.6 may also use a temperature monitoring means 48,50 as shown in Fig.5.

### The Embodiment of Fig.7

[0047] Fig.7 shows another alternative embodiment of the invention wherein the balloon is a double-wall balloon having a non-porous inner wall 28A, and a porous outer wall 28B. The first subcutaneously implantable receptacle 30 and catheter 32 previously described communicate with the non-porous inner wall 28A for providing the first treatment fluid 44 to the interior of the inner wall 28A. The first treatment fluid 44 is preferably a radioactive treatment fluid. The heating means 46 previously described is provided for non-invasive heating of the first treatment fluid 44. The alternative heating means of Fig.6 could also be utilized.

[0048] A second subcutaneously implantable receptacle means 68 is provided for receiving a transdermal injection of a second treatment fluid 70, which preferably is a chemotherapy treatment fluid 70. The second receptacle 68 may be held in place by suture tabs such as 69. A second catheter 72 communicates the second receptacle 68 with the space 74 defined between the inner and outer walls 28A and 28B within which the chemotherapy fluid 70 is received. The space 74 preferably has a layer of sponge-like material 76 lying therein between the inner and outer walls 28A and 28B for temporarily holding the chemotherapy fluid 70 therein.

[0049] The porous outer wall 28B includes numerous small openings 78 therein allowing the chemotherapy fluid 70 to seep out such as in droplets 80. The chemotherapy fluid seeps out the porous outer wall 28B into direct contact with the brain tissue 16 surrounding the cavity 24.

[0050] The previously described crystal oscillator 48 may be placed within either the inner wall 28A or within the outer wall 28B for monitoring of the temperature of the fluids therein as previously described.

[0051] A check valve 82 may be disposed in the second catheter 72 for preventing flow of the chemotherapy fluid 70 back therethrough from space 74 back to receptacle 68. The one-way check valve 82 is available from Halkey-Roberts Corporation of St. Petersburg, Florida, and may for example be constructed in accordance with the teachings of U.S. Patent No. 4,681,132 to Lardner.

[0052] It will be appreciated that fluid pressures both from the first fluid 44 within the inner wall 28A and the second fluid 70 with the space 74 will act to urge the second fluid 70 out through the small openings 78 in the porous outer wall 28B.

[0053] Fig.7 illustrates a treatment means including heating means 46 and the first and second subcutaneous receptacles 30 and 68 operably associated with the balloon means 28A,28B for simultaneously non-invasively applying at least two, and if preferred all three, treatment modalities from the group consisting of radiation, heat and chemotherapy to remaining brain tissue 16 surrounding cavity 24.

[0054] Alternatively, instead of use of a double-wall balloon 28A,28B chemotherapy alone could be applied

with a structure like that shown in Fig.5 wherein the outer wall 28 is a porous wall and wherein the interior thereof contains a sponge-like material.

### The Embodiment of Fig.8

[0055] Fig.8 illustrates a balloon 28 like that of Fig.5 and also illustrates the fact that certain aspects of the present invention can be achieved without the use of the subcutaneously implanted receptacle 30, but instead by having a transdermal catheter 84 extend through the skull 14 and scalp 12 by means of a hollow bolt 86 implanted in the skull 14 which has the transdermal catheter 84 sealingly and securely disposed there-through. The hollow bolt 86 may if desired be made of non-metallic materials.

### The Embodiment of Figs.9 and 10

[0056] Figs 9 and 10 illustrate another embodiment of the invention. In Fig.9 a modified subcutaneously implantable receptacle 88 is illustrated. It is connected to balloon 28 by catheter 32.

[0057] It will be appreciated that the subcutaneously implantable reservoir 30 shown in Figs. 1-7 is designed such that the overlying scalp 12 is somewhat deformed to accommodate the size of the subcutaneous receptacle 30. The subcutaneous receptacle 30 of Figs. 1-7 is typically located by palpation of the scalp 40 so as to locate the subcutaneous reservoir 30 by feel. It will be appreciated that a palpable receptacle such as receptacle 30 implies pressure upon the overlying scalp 12 which may compromise blood supplied to the scalp 12 in that area, hence potentially causing skin necrosis or breakdown, a definite disadvantage.

[0058] The modified receptacle 88 is circular in shape and includes an annular metallic ring 90 which is impenetrable by X-rays. The receptacle 88 and metallic ring 90 are placed with a counterbore 92 which is formed within the skull 14 with commonly utilized air-driven drills such as that manufactured by the Midas Rex Company. The receptacle 88 may be held in place by suture tabs 94. It may also be held in place by conventional threaded screws (not shown) screwed into the skull 14.

[0059] The modified receptacle 88 may be installed in such a manner so as not to deform the overlying scalp 12 or create undue pressure upon the scalp 12. It does, however, present a need for an easy means of accurately locating the subcutaneous receptacle 88 so that treatment fluids may be injected therein with hypodermic needle similar to the process illustrated in Fig.4. This localisation is accomplished as shown in Fig. 10.

[0060] A metallic grid 94 is laid in place over the patient's scalp 12 and may be held fixedly in place thereon by means such as tape 96. Next, a plain en face radiograph, i.e. X-ray, of scalp, reservoir, grid and skull is taken. By observing the X-ray film, the relationship between the external metallic grid 94 and the subcuta-

neous metallic ring 90 may be easily seen, allowing selection of the correct grid square externally through which the hypodermic needle 40 can be successfully passed to hit the centre of the subcutaneous receptacle 88.

### Claims

1. A chemotherapy apparatus (10) for treatment of tissue surrounding a cavity (24) left by a surgical excision, comprising:

a distensible inner reservoir (28A) and outer reservoir (28B), the outer reservoir comprising a porous wall and the inner reservoir comprising a non-porous wall, the inner and outer reservoirs arranged so that a space is defined between them;

a first catheter (32) connected to the space between the inner and outer reservoirs for delivery of a chemotherapy fluid into the space; and

a second catheter (72) connected to the inner reservoir for delivery of a second fluid into the inner reservoir.

2. The apparatus according to claim 1, further comprising a first and second fluid receptacle (44,68) connected to the first and second catheter for receiving transdermal injections of the chemotherapy fluid and the second fluid, respectively.

3. The apparatus according to claim 2, wherein the first and second receptacles are implanted subcutaneously.

4. The apparatus according to claim 1, 2 or 3, wherein the space between inner and outer reservoirs comprises a sponge (76) for temporarily holding the chemotherapy fluid.

5. The apparatus according any preceding claim, wherein the second fluid comprises a radioactive treatment fluid.

6. The apparatus according to claim 5, wherein the radioactive treatment fluid comprises a radioisotope selected from the group consisting of <sup>90</sup>-Yttrium, <sup>198</sup>-Gold, <sup>32</sup>-Phosphorus, <sup>125</sup>-Iodine and <sup>131</sup>-Iodine.

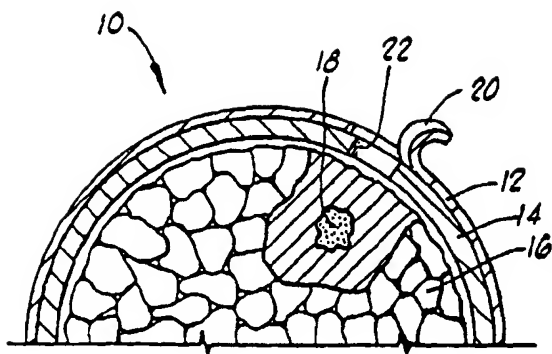
7. The apparatus according to claim 5 or 6, wherein the outer reservoir includes means for spacing the inner reservoir from the tissue surrounding the cavity when the inner reservoir is filled with radioactive treatment fluid and the outer reservoir is filled with chemotherapy fluid.

8. The apparatus of claims 1 to 7, further comprising an external energy transmitter for simultaneous application of heat energy to the tissue surrounding a cavity left by a surgical excision.

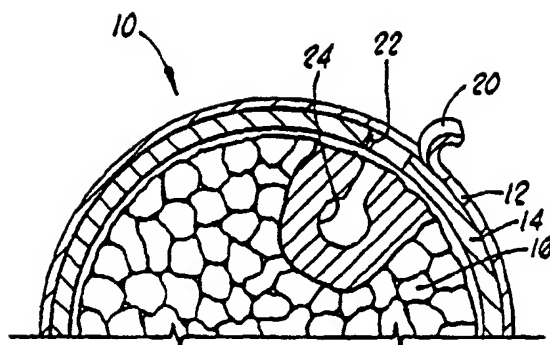
9. The apparatus of claim 8, wherein the external energy transmitter is an ultrasonic transmitter, microwave transmitter or radio frequency transmitter.

10. The apparatus of claim 8, further comprising a temperature monitor (48) in thermal communication with at least one of the reservoirs, the temperature monitor generating a signal responsive to the temperature of a fluid in the reservoir.

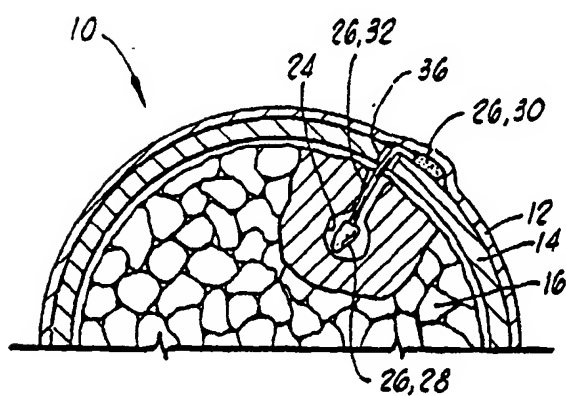




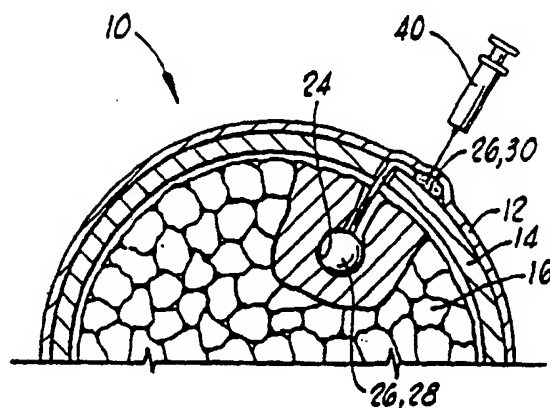
**FIG. 1**



**FIG. 2**



**FIG. 3**



**FIG. 4**



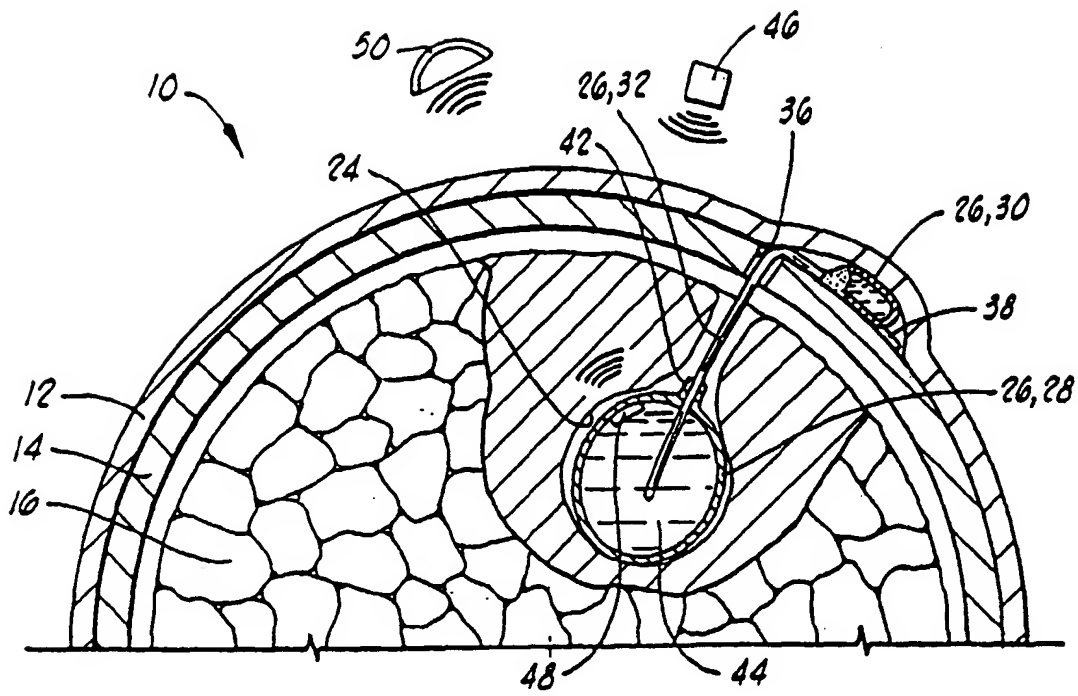


FIG. 5

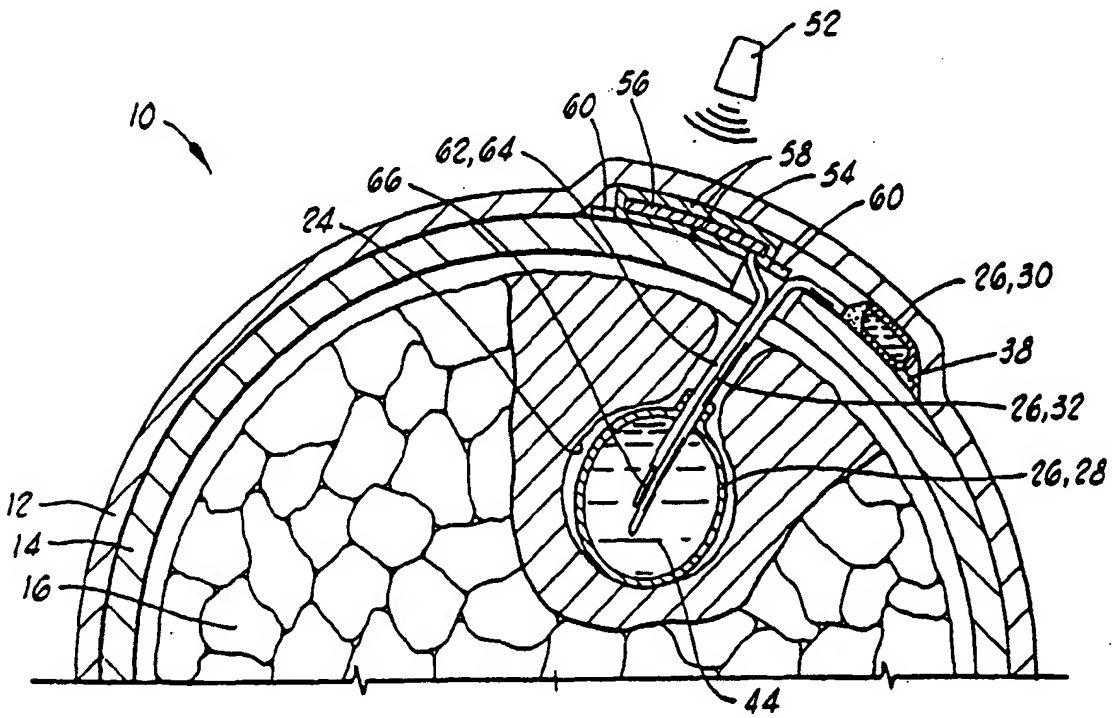
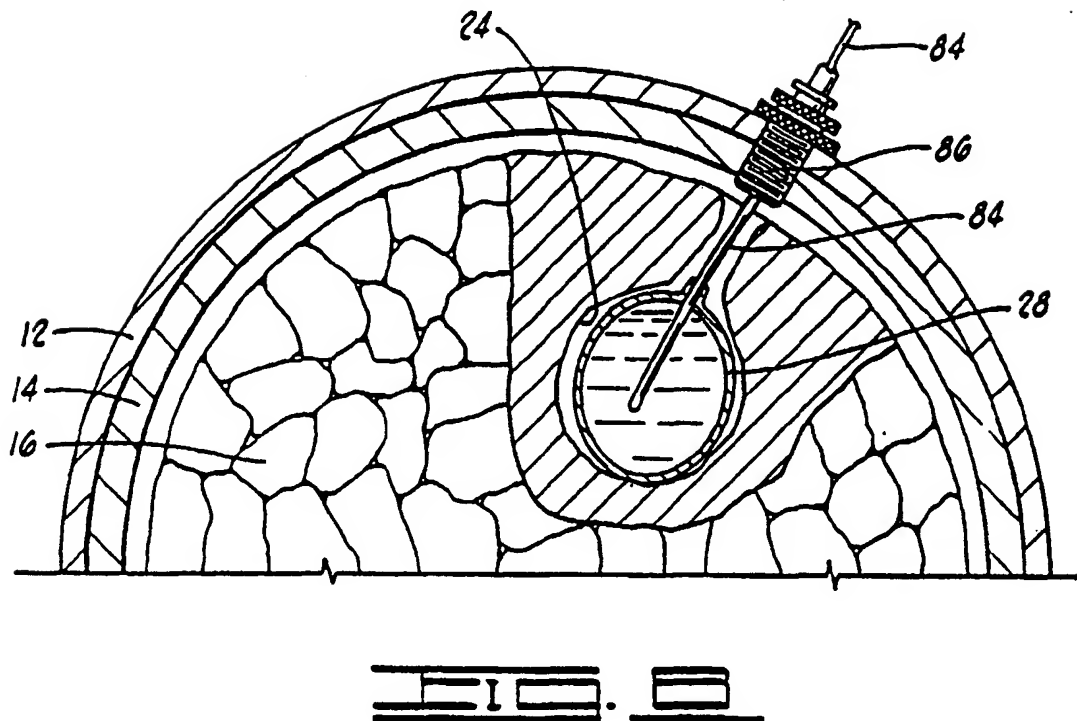
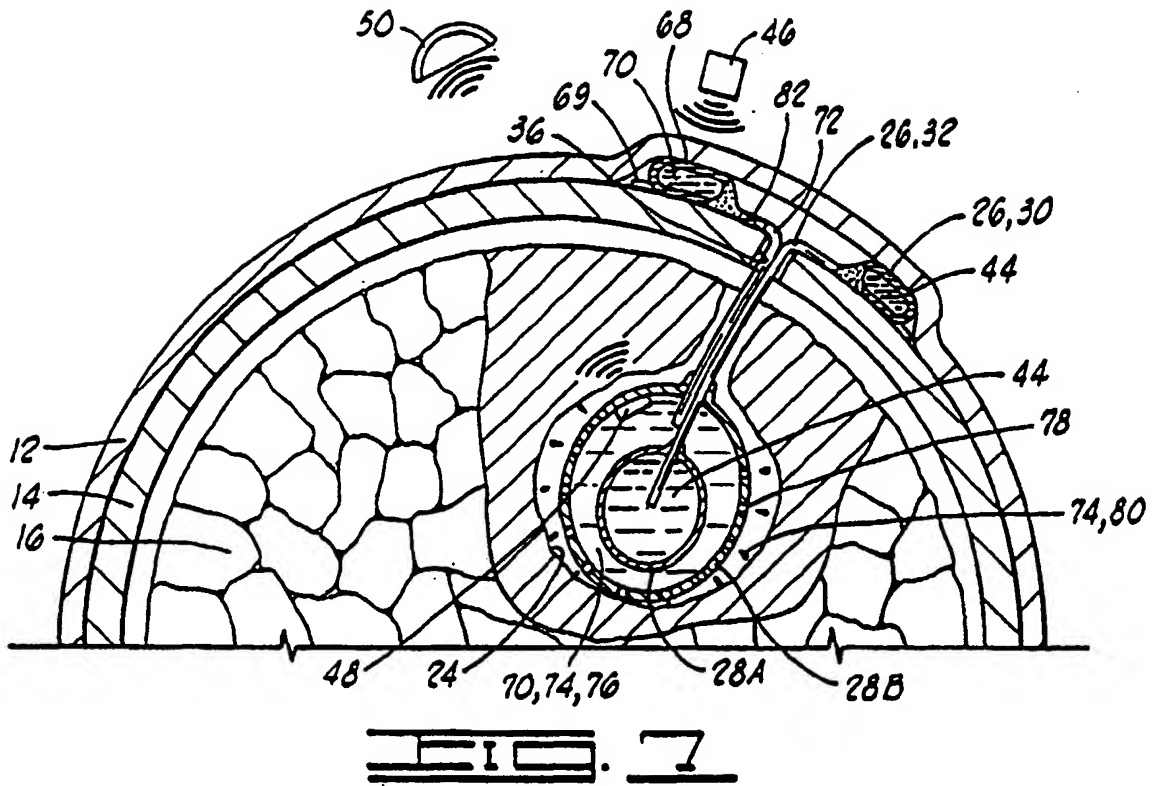


FIG. 6



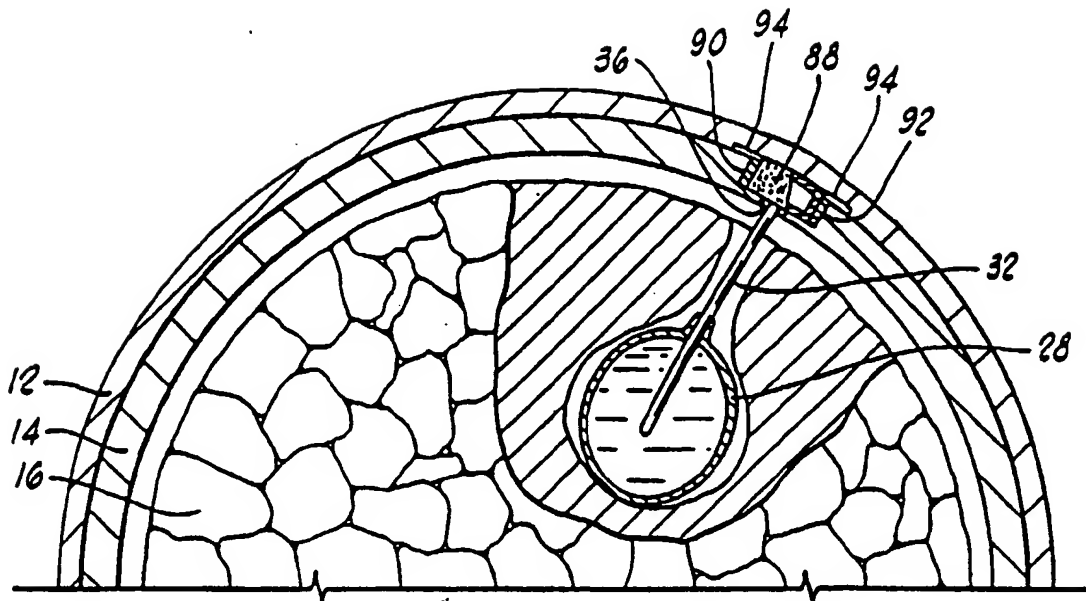


FIG. 9

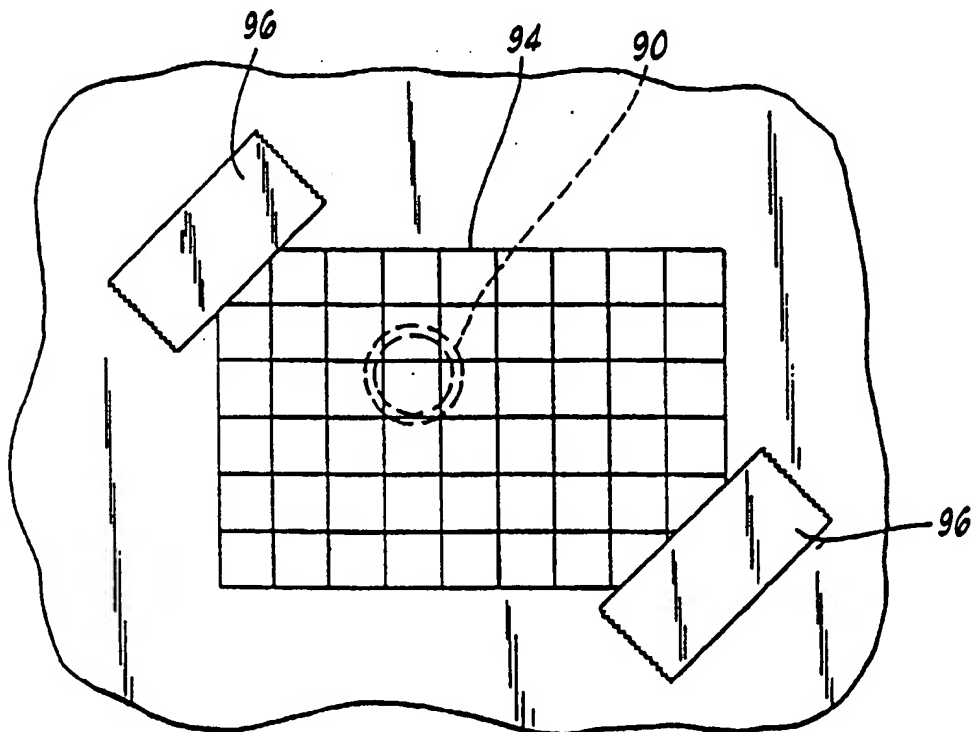


FIG. 10



(19)



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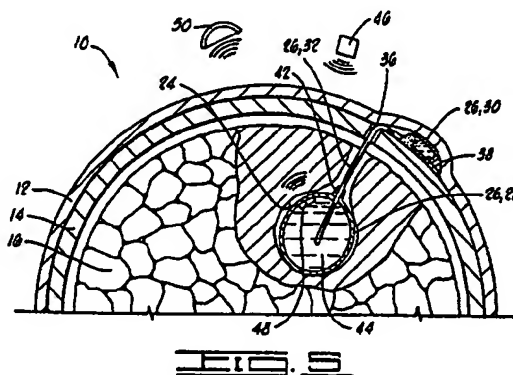
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**(54) Tumour treatment apparatus**

(57) A chemotherapy apparatus (10) for treatment of tissue surrounding a cavity (24) left by a surgical excision, comprises:

a distensible inner reservoir (28A) and outer reservoir (28B), the outer reservoir comprising a porous wall and the inner reservoir comprising a non-porous wall, the inner and outer reservoirs arranged so that a space is defined between them; a first catheter (32) connected to the space between the inner and outer reservoirs for delivery of a chemotherapy fluid into the space; and a second catheter (72) connected to the inner reservoir for delivery of a second fluid into the inner reservoir.



**EP 0 970 724 A3**



European Patent  
Office

# EUROPEAN SEARCH REPORT

Application Number  
EP 99 11 9829

DOCUMENTS CONSIDERED TO BE RELEVANT					
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.7)		
X	US 4 417 576 A (BARAN OSTAP E) 29 November 1983 (1983-11-29) * abstract *	1,4,7	A61N5/02 A61M39/02		
Y	---	2,3,8-10			
X	EP 0 399 712 A (SCHNEIDER USA INC) 28 November 1990 (1990-11-28) * column 2, line 17 - line 53 * * column 3, line 8 - line 51 * * column 4, line 34 - column 5, line 8 *	1			
Y	US 3 640 269 A (DELGADO JOSE M R) 8 February 1972 (1972-02-08) * column 2, line 44 - column 3, line 11 *	2,3			
Y	US 4 989 601 A (MORAN CHRISTOPHER J ET AL) 5 February 1991 (1991-02-05) * column 2, line 41 - line 51 * * column 1, line 37 - line 40 * * column 3, line 48 - column 4, line 25 *	8-10			
A	EP 0 383 429 A (BARD INC C R) 22 August 1990 (1990-08-22) * abstract * * page 5, line 37 - line 43 *	1	<table border="1"> <thead> <tr> <th>TECHNICAL FIELDS SEARCHED (Int.Cl.7)</th> </tr> </thead> <tbody> <tr> <td>A61M A61N</td> </tr> </tbody> </table>	TECHNICAL FIELDS SEARCHED (Int.Cl.7)	A61M A61N
TECHNICAL FIELDS SEARCHED (Int.Cl.7)					
A61M A61N					
The present search report has been drawn up for all claims					
Place of search <b>THE HAGUE</b>		Date of completion of the search <b>10 October 2000</b>	Examiner <b>Petter, E</b>		
<table border="0"> <tr> <td> <b>CATEGORY OF CITED DOCUMENTS</b>  X : particularly relevant if taken alone  Y : particularly relevant if combined with another document of the same category  A : technological background  O : non-written disclosure  P : intermediate document </td> <td> T : theory or principle underlying the invention  E : earlier patent document, but published on, or after the filing date  D : document cited in the application  L : document cited for other reasons    &amp; : member of the same patent family, corresponding document </td> </tr> </table>				<b>CATEGORY OF CITED DOCUMENTS</b> X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document	T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons  & : member of the same patent family, corresponding document
<b>CATEGORY OF CITED DOCUMENTS</b> X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document	T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons  & : member of the same patent family, corresponding document				

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**ANNEX TO THE EUROPEAN SEARCH REPORT  
ON EUROPEAN PATENT APPLICATION NO.**

EP 99 11 9829

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The members are as contained in the European Patent Office EDP file on  
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

10-10-2000

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
US 4417576	A	29-11-1983	NONE		
EP 0399712	A	28-11-1990	US	4994033 A	19-02-1991
			AT	103499 T	15-04-1994
			AU	611077 B	30-05-1991
			AU	5595690 A	06-12-1990
			CA	2017319 A,C	25-11-1990
			DE	9005882 U	08-11-1990
			DE	69007674 D	05-05-1994
			DE	69007674 T	14-07-1994
			DK	399712 T	16-05-1994
			ES	2050370 T	16-05-1994
			IE	63848 B	14-06-1995
			IL	94439 A	15-03-1995
			JP	1777087 C	28-07-1993
			JP	3007169 A	14-01-1991
			JP	4064709 B	15-10-1992
			KR	9302271 B	27-03-1993
			NO	902292 A	26-11-1990
			PT	94150 A,B	08-01-1991
US 3640269	A	08-02-1972	NONE		
US 4989601	A	05-02-1991	US	4961422 A	09-10-1990
			AT	133547 T	15-02-1996
			CA	1336317 A	18-07-1995
			DE	68925553 D	14-03-1996
			DE	68925553 T	05-06-1996
			EP	0361762 A	04-04-1990
			ES	2088896 T	01-10-1996
			JP	2191469 A	27-07-1990
			JP	2876135 B	31-03-1999
			US	4947842 A	14-08-1990
			AT	119018 T	15-03-1995
			AU	650125 B	09-06-1994
			AU	1527192 A	25-06-1992
			AU	619711 B	30-01-1992
			AU	2806489 A	23-05-1989
			CA	1328905 A	26-04-1994
			DE	3853215 D	06-04-1995
			DK	98790 A	20-04-1990
			EP	0382787 A	22-08-1990
			JP	3501816 T	25-04-1991
			WO	8903665 A	05-05-1989
			US	5197466 A	30-03-1993

EPO FORM P4459

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82



**ANNEX TO THE EUROPEAN SEARCH REPORT  
ON EUROPEAN PATENT APPLICATION NO.**

EP 99 11 9829

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report.  
The members are as contained in the European Patent Office EDP file on  
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

10-10-2000

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0383429 A	22-08-1990	CA 2008915 A, C	31-07-1990
		DE 69023362 D	14-12-1995
		DE 69023362 T	04-04-1996
		ES 2078936 T	01-01-1996
		JP 2283380 A	20-11-1990
		JP 2935522 B	16-08-1999
		US 5087244 A	11-02-1992
<hr/>			

EPO FORM P0459

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82